PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C07K — A2

(11) International Publication Number: **WO 99/46281**

(43) International Publication Date: 16 September 1999 (16.09.99)

(21) International Application Number: PCT/US99/05028

(22) International Filing Date: 8 March 1999 (08.03.99)

(30) Priority Data:

60/077,450	10 March 1998 (10.03.98)	US
60/077,632	11 March 1998 (11.03.98)	US
60/077,641	11 March 1998 (11.03.98)	US

(Continued on the following page)

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(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

Without international search report and to be republished upon receipt of that report.

(54) Title: NOVEL POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME

(57) Abstract

The present invention is directed to novel polypeptides and to nucleic acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

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(Continued)

(30) 60/077,450	10 Mar/mar 1998 (10.03.1998)	US	(30) 60/081,049	8 Apr/avr 1998 (08.04.1998)	US	(30) 60/084,414	6 May/mai 1998 (06.05.1998)	US
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(30) 60/077,641	11 Mar/mar 1998 (11.03.1998)	US	(30) 60/081,203	9 Apr/avr 1998 (09.04.1998)	US	(30) 60/084,639	7 May/mai 1998 (07.05.1998)	US
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(30) 60/078,004	13 Mar/mar 1998 (13.03.1998)	US	(30) 60/081,955	15 Apr/avr 1998 (15.04.1998)	US	(30) 60/084,598	7 May/mai 1998 (07.05.1998)	US
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(30) 60/078,886	20 Mar/mar 1998 (20.03.1998)	US	(30) 60/081,817	15 Apr/avr 1998 (15.04.1998)	US	(30) 60/084,627	7 May/mai 1998 (07.05.1998)	US
(30) 60/078,910	20 Mar/mar 1998 (20.03.1998)	US	(30) 60/082,569	21 Apr/avr 1998 (21.04.1998)	US	(30) 60/085,339	13 May/mai 1998 (13.05.1998)	US
(30) 60/078,939	20 Mar/mar 1998 (20.03.1998)	US	(30) 60/082,568	21 Apr/avr 1998 (21.04.1998)	US	(30) 60/085,338	13 May/mai 1998 (13.05.1998)	US
(30) 60/078,936	20 Mar/mar 1998 (20.03.1998)	US	(30) 60/082,700	22 Apr/avr 1998 (22.04.1998)	US	(30) 60/085,323	13 May/mai 1998 (13.05.1998)	US
(30) 60/079,294	25 Mar/mar 1998 (25.03.1998)	US	(30) 60/082,804	22 Apr/avr 1998 (22.04.1998)	US	(30) 60/085,573	15 May/mai 1998 (15.05.1998)	US
(30) 60/079,656	26 Mar/mar 1998 (26.03.1998)	US	(30) 60/082,704	22 Apr/avr 1998 (22.04.1998)	US	(30) 60/085,697	15 May/mai 1998 (15.05.1998)	US
(30) 60/079,728	27 Mar/mar 1998 (27.03.1998)	US	(30) 60/082,767	23 Apr/avr 1998 (23.04.1998)	US	(30) 60/085,580	15 May/mai 1998 (15.05.1998)	US
(30) 60/079,786	27 Mar/mar 1998 (27.03.1998)	US	(30) 60/082,796	23 Apr/avr 1998 (23.04.1998)	US	(30) 60/085,579	15 May/mai 1998 (15.05.1998)	US
(30) 60/079,664	27 Mar/mar 1998 (27.03.1998)	US	(30) 60/083,336	27 Apr/avr 1998 (27.04.1998)	US	(30) 60/085,704	15 May/mai 1998 (15.05.1998)	US
(30) 60/079,689	27 Mar/mar 1998 (27.03.1998)	US	(30) 60/083,322	28 Apr/avr 1998 (28.04.1998)	US	(30) 60/085,582	15 May/mai 1998 (15.05.1998)	US
(30) 60/079,663	27 Mar/mar 1998 (27.03.1998)	US	(30) 60/083,392	29 Apr/avr 1998 (29.04.1998)	US	(30) 60/085,689	15 May/mai 1998 (15.05.1998)	US
(30) 60/079,923	30 Mar/mar 1998 (30.03.1998)	US	(30) 60/083,499	29 Apr/avr 1998 (29.04.1998)	US	(30) 60/085,700	15 May/mai 1998 (15.05.1998)	US
(30) 60/079,920	30 Mar/mar 1998 (30.03.1998)	US	(30) 60/083,545	29 Apr/avr 1998 (29.04.1998)	US	(30) 60/086,023	18 May/mai 1998 (18.05.1998)	US
(30) 60/080,105	31 Mar/mar 1998 (31.03.1998)	US	(30) 60/083,554	29 Apr/avr 1998 (29.04.1998)	US	(30) 60/086,486	22 May/mai 1998 (22.05.1998)	US
(30) 60/080,165	31 Mar/mar 1998 (31.03.1998)	US	(30) 60/083,495	29 Apr/avr 1998 (29.04.1998)	US	(30) 60/086,414	22 May/mai 1998 (22.05.1998)	US
(30) 60/080,194	31 Mar/mar 1998 (31.03.1998)	US	(30) 60/083,558	29 Apr/avr 1998 (29.04.1998)	US	(30) 60/086,392	22 May/mai 1998 (22.05.1998)	US
(30) 60/080,107	31 Mar/mar 1998 (31.03.1998)	US	(30) 60/083,496	29 Apr/avr 1998 (29.04.1998)	US	(30) 60/086,430	22 May/mai 1998 (22.05.1998)	US
(30) 60/080,333	1 Apr/avr 1998 (01.04.1998)	US	(30) 60/083,559	29 Apr/avr 1998 (29.04.1998)	US	(30) 60/087,208	28 May/mai 1998 (28.05.1998)	US
(30) 60/080,327	1 Apr/avr 1998 (01.04.1998)	US	(30) 60/083,500	29 Apr/avr 1998 (29.04.1998)	US	(30) 60/087,098	28 May/mai 1998 (28.05.1998)	US
(30) 60/080,334	1 Apr/avr 1998 (01.04.1998)	US	(30) 60/083,742	30 Apr/avr 1998 (30.04.1998)	US	(30) 60/087,106	28 May/mai 1998 (28.05.1998)	US
(30) 60/080,328	1 Apr/avr 1998 (01.04.1998)	US	(30) 60/084,366	5 May/mai 1998 (05.05.1998)	US	(30) 60/094,651	30 Jul/juil 1998 (30.07.1998)	US
(30) 60/081,071	8 Apr/avr 1998 (08.04.1998)	US	(30) 60/084,441	6 May/mai 1998 (06.05.1998)	US	(30) 60/100,038	11 Sep/sep 1998 (11.09.1998)	US
(30) 60/081,070	8 Apr/avr 1998 (08.04.1998)	US						

immune complexes from patients plasma *in vivo* (Lim et al., Biochem. Biophys. Res. Commun. 218:260-266 (1996)). We herein describe the identification and characterization of a novel polypeptide having homology to the conglutinin protein, designated herein as PRO702.

15. PRO703

Very-long-chain acyl-CoA synthetase ("VLCAS") is a long-chain fatty acid transport protein which is active in the cellular transport of long and very long chain fatty acids. [see for example, Uchida et al., J Biochem (Tokyo) 119(3):565-571 (1996) and Uchiyama et al., J Biol Chem 271(48):30360-30365 (1996). Given the biological importance of fatty acid transport mechanisms, efforts are currently being under taken to identify new, native proteins which are involved in fatty acid transport. We describe herein the identification of a novel polypeptide which has homology to VLCAS, designated herein as PRO703.

16. PRO705

The glypicans are a family of glycosylphosphatidylinositol (GPI)-anchored proteoglycans that, by virtue of their cell surface localization and possession of heparin sulfate chains, may regulate the responses of cells to numerous heparin-binding growth factors, cell adhesion molecules and extracellular matrix components. Mutations in one glypican protein cause of syndrome of human birth defects, suggesting that the glypicans may play an important role in development (Litwack et al., Dev. Dyn. 211:72-87 (1998)). Also, since the glypicans may interact with the various extracellular matrices, they may also play important roles in wound healing (McGrath et al., Pathol. 183:251-252 (1997)). Furthermore, since glypicans are expressed in neurons and glioma cells, they may also play an important role in the regulation of cell division and survival of cells of the nervous system (Liang et al., J. Cell. Biol. 139:851-864 (1997)). It is evident, therefore, that the glypicans are an extremely important family of proteoglycans. There is, therefore, substantial interest in identifying novel polypeptides having homology to members of the glypican family. We herein describe the identification and characterization of a novel polypeptide having homology to K-glypican, designated herein as PRO705.

17. PRO708

Aryl sulfatases are enzymes that exist in a number of different isoforms, including aryl sulfatase A (ASA), aryl sulfatase B (ASB) and aryl sulfatase C (ASC), and that function to hydrolyze a variety of different aromatic sulfates. Aryl sulfatases have been isolated from a variety of different animal tissues and microbial sources and their structures and functions have been extensively studied (see, e.g., Nichol and Roy, J. Biochem. 55:643-651 (1964)). ASA deficiency has been reported to be associated with metachromatic leukodystrophy (MLD) (Giles et al., Prenat. Diagn. 7(4):245-252 (1987) and Herska et al., Am. J. Med. Genet. 26(3):629-635 (1987)). Additionally, other groups have reported that aryl sulfatases have been found in high levels in natural killer cells of the immune system and have hypothesized a possible role for these enzymes in NK cell-mediated cellular lysis (see, e.g., Zucker-Franklin et al., Proc. Natl. Acad. Sci. USA 80(22):6977-6981 (1983)). Given the obvious physiological importance of the aryl sulfatase enzymes, there is a substantial interest in identifying novel aryl sulfatase homolog polypeptides. We herein describe the identification and characterization of novel polypeptides having homology to the aryl sulfatases, wherein these n vel polypeptides are herein designated PRO708 polypeptides.

EXAMPLE 113: In Vitro Antiproliferative Assay

The antiproliferative activity of various PRO polypeptides was determined in the investigational, disease-oriented *in vitro* anti-cancer drug discovery assay of the National Cancer Institute (NCI), using a sulforhodamine B (SRB) dye binding assay essentially as described by Skehan et al., *J. Natl. Cancer Inst.* 82:1107-1112 (1990). Th 60 tumor cell lines employed in this study ("the NCI panel"), as well as conditions for their maintenance and culture *in vitro* have been described by Monks et al., *J. Natl. Cancer Inst.* 83:757-766 (1991). The purpose of this screen is to initially evaluate the cytotoxic and/or cytostatic activity of the test compounds against different types of tumors (Monks et al., *supra*; Boyd, *Cancer: Princ. Pract. Oncol. Update* 3(10):1-12 [1989]).

Cells from approximately 60 human tumor cell lines were harvested with trypsin/EDTA (Gibco), washed once, resuspended in IMEM and their viability was determined. The cell suspensions were added by pipet (100 μL volume) into separate 96-well microtiter plates. The cell density for the 6-day incubation was less than for the 2-day incubation to prevent overgrowth. Inoculates were allowed a preincubation period of 24 hours at 37°C for stabilization. Dilutions at twice the intended test concentration were added at time zero in 100 μL aliquots to the microtiter plate wells (1:2 dilution). Test compounds were evaluated at five half-log dilutions (1000 to 100,000-fold). Incubations took place for two days and six days in a 5% CO_2 atmosphere and 100% humidity.

After incubation, the medium was removed and the cells were fixed in 0.1 ml of 10% trichloroacetic acid at 40°C. The plates were rinsed five times with deionized water, dried, stained for 30 minutes with 0.1 ml of 0.4% sulforhodamine B dye (Sigma) dissolved in 1% acetic acid, rinsed four times with 1% acetic acid to remove unbound dye, dried, and the stain was extracted for five minutes with 0.1 ml of 10 mM Tris bas [tris(hydroxymethyl)aminomethane], pH 10.5. The absorbance (OD) of sulforhodamine B at 492 nm was measured using a computer-interfaced, 96-well microtiter plate reader.

A test sample is considered positive if it shows at least 50% growth inhibitory effect at one or more concentrations. The following PRO polypeptides gave positive results in at least one tumor cell line: PRO181, PRO237, PRO526, PRO362 and PRO866.

EXAMPLE 114: Gene Amplification

This example shows that genes encoding various PRO polypeptides are amplified in the genome of certain human cancers. Amplification is associated with overexpression of the gene product, indicating that the PRO polypeptide is a useful target for therapeutic intervention in certain cancers such as colon, lung and other cancers. Therapeutic agent may take the form of antagonists of PRO polypeptide-encoding genes, for example, murine-human chimeric, humanized or human antibodies against the PRO polypeptide.

The starting material for the screen was genomic DNA isolated from a variety cancers. The DNA is quantitated precisely, e.g., fluorometrically. As a negative control, DNA was isolated from the cells of ten normal healthy individuals which was pooled and used as assay controls for the gene copy in healthy individuals (NorHu).

The 5' nuclease assay (for example, TaqMan™) and real-time quantitative PCR (for example, ABI Prizm 7700 Sequence Detection System™ (Perkin Elmer, Applied Biosystems Division, Foster City, CA)), were used to find genes potentially amplified in certain cancers. The results were used to determine whether the DNA encoding the PRO polypeptide is over-represented in any of the lung and colon cancers that were screened. The result was reported in Delta CT units. One unit corresponds 1 PCR cycle or approximately a 2-fold amplification relative to normal, two units corresponds to 4-fold, 3 units to 8-fold and so on. Quantitation was obtained using primers and

a Taqman™ fluorescent derived from the PRO polypeptide-encoding gene. Regions of the PRO polypeptide which are most likely to contain unique nucleic acid sequences and which are least likely to have spliced ut introns are preferred for the primer derivation, e.g., 3'-untranslated region.

The 5' nuclease assay reaction is a fluorescent PCR-based technique which makes use of the 5' exonuclease activity of Taq DNA polymerase enzyme to monitor amplification in real time. Two oligonucleotide primers are used to generate an amplicon typical of a PCR reaction. A third oligonucleotide, or probe, is designed to detect nucleotide sequence located between the two PCR primers. The probe is non-extendible by Taq DNA polymerase enzyme, and is labeled with a reporter fluorescent dye and a quencher fluorescent dye. Any laser-induced emission from the reporter dye is quenched by the quenching dye when the two dyes are located close together as they are on the probe. During the amplification reaction, the probe is cleaved by the Taq DNA polymerase enzyme in a template-dependent manner. The resultant probe fragments disassociate in solution, and signal from the released reporter dye is free from the quenching effect of the second fluorophore. One molecule of reporter dye is liberated for each new molecule synthesized, and detection of the unquenched reporter dye provides the basis for quantitative interpretation of the data.

The 5' nuclease procedure is run on a real-time quantitative PCR device such as the ABI Prism 7700TM Sequence Detection. The system consists of a thermocyler, laser, charge-coupled device (CCD) camera and computer. The system amplifies samples in a 96-well format on a thermocycler. During amplification, laser-induced fluorescent signal is collected in real-time through fiber optics cables for all 96 wells, and detected at the CCD. The system includes software for running the intrument and for analyzing the data.

5' Nuclease assay data are initially expressed as Ct, or the threshold cycle. This is defined as the cycle at which the reporter signal accumulates above the background level of fluorescence. The Ct values are used as quantitative measurement of the relative number of starting copies of a particular target sequence in a nucleic acid sample.

Genes encoding the following PRO polypeptides were found to be amplified in the above assay: PRO213-1, PRO237, PRO324, PRO351, PRO362, PRO853, PRO615, PRO531, PRO618, PRO772, PRO703, PRO474, PRO1017 and PRO792.

EXAMPLE 115: Induction of c-fos in Endothelial Cells

Human venous umbilical vein endothelial cells (HUVEC, Cell Systems) in growth media (50:50 without glycine, 1% glutamine, 10mM Hepes, 10% FBS, 10 ng/ml bFGF), were plated on 96-well microtiter plates at a cell density of $1x10^4$ cells/well. The day after plating, the cells were starved by removing the growth media and treating the cells with 100 µl/well test samples and controls (positive control: growth media; negative control: Protein 32). The cells were incubated for 30 minutes at 37°C, in 5% CO_2. The samples were removed, and the first part of the bDNA kit protocol (Chiron Diagnostics, cat. #6005-037) was followed.

Briefly, the amounts of the TM Lysis Buffer and Probes needed for the tests were calculated based on information provided by the manufacturer. The appropriate amounts of thawed Probes were added to the TM Lysis Buffer. The Capture Hybridization Buffer was warmed to room temperature. The bDNA strips were set up in the metal strip holders, and 100 µl of Capture Hybridization Buffer were added to each b-DNA well needed, followed by incubation for at least 30 minutes. The test plates with the cells were removed from the incubator, and the media was gently removed using the vacuum manifold. 100µl of Lysis Hybridization Buffer with Probes were quickly pipetted into each well of the micr titer plates. The plates were then incubated at 55°C for 15 minutes. Upon

FIGURE 39

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA50913
><subunit 1 of 1, 730 aa, 1 stop
><MW: 78644, pI: 7.65, NX(S/T): 2
MGVCQRTRAPWKEKSQLERAALGFRKGGSGMFASGWNQTVPIEEAGSMAALLLLPLLLLLPL
LLLKLHLWPQLRWLPADLAFAVRALCCKRALRARALAAAAADPEGPEGGCSLAWRLAELAQQ
RAAHTFLIHGSRRFSYSEAERESNRAARAFLRALGWDWGPDGGDSGEGSAGEGERAAPGAGD
AAAGSGAEFAGGDGAARGGGAAAPLSPGATVALLLPAGPEFLWLWFGLAKAGLRTAFVPTAL
RRGPLLHCLRSCGARALVLAPEFLESLEPDLPALRAMGLHLWAAGPGTHPAGISDLLAEVSA
EVDGPVPGYLSSPQSITDTCLYIFTSGTTGLPKAARISHLKILQCQGFYQLCGVHQEDVIYL
ALPLYHMSGSLLGIVGCMGIGATVVLKSKFSAGQFWEDCQQHRVTVFQYIGELCRYLVNQPP
SKAERGHKVRLAVGSGLRPDTWERFVRRFGPLQVLETYGLTEGNVATINYTGQRGAVGRASW
LYKHIFPFSLIRYDVTTGEPIRDPQGHCMATSPGEPGLLVAPVSQQSPFLGYAGGPELAQGK
LLKDVFRPGDVFFNTGDLLVCDDQGFLRFHDRTGDTFRWKGENVATTEVAEVFEALDFLQEV
NVYGVTVPGHEGRAGMAALVLRPPHALDLMQLYTHVSENLPPYARPRFLRLQESLATTETFK
QQKVRMANEGFDPSTLSDPLYVLDQAVGAYLPLTTARYSALLAGNLRI

Signal peptide:
aa 1-42

cAMP- and cGMP-dependent protein kinase phosphorylation site
starting at aa 136

CUB domain protein motif
aa 254-261

putative AMP-binding domain siganture
aa 332-343

N-glycosylation sites
aa 37-40 and 483-486

WHAT IS CLAIMED IS:

1. Isolated nucleic acid having at least 80% sequence identity to a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:7), Figure 9 (SEQ ID NO:19), Figure 11 (SEQ ID NO:28), Figure 15 (SEQ ID NO:36), Figure 20 (SEQ ID NO:45), Figure 22 (SEQ ID NO:52), Figure 24 (SEQ ID NO:59), Figure 26 (SEQ ID NO:64), Figure 28 (SEQ ID NO:69), Figure 30 (SEQ ID NO:74), Figure 33 (SEQ ID NO:85), Figure 35 (SEQ ID NO:90), Figure 37 (SEQ ID NO:97), Figure 39 (SEQ ID NO:102), Figure 41 (SEQ ID NO:109), Figure 43 (SEQ ID NO:114), Figure 45 (SEQ ID NO:119), Figure 47 (SEQ ID NO:124), Figure 49 (SEQ ID NO:132), Figure 51 (SEQ ID NO:137), Figure 53 (SEQ ID NO:145), Figure 55 (SEQ ID NO:150), Figure 59 (SEQ ID NO:157), Figure 61 (SEQ ID NO:162), Figure 63 (SEQ ID NO:169), Figure 66 (SEQ ID NO:178), Figure 68 (SEQ ID NO:183), Figure 70 (SEQ ID NO:190), Figure 73 (SEQ ID NO:196), Figure 75 (SEQ ID NO:206), Figure 77 (SEQ ID NO:211), Figure 79 (SEQ ID NO:216), Figure 81 (SEQ ID NO:221), Figure 83 (SEQ ID NO:226), Figure 85 (SEQ ID NO:231), Figure 87 (SEQ ID NO:236), Figure 89 (SEQ ID NO:245), Figure 91 (SEQ ID NO:254), Figure 93 (SEQ ID NO:259), Figure 95 (SEQ ID NO:264), Figure 98 (SEQ ID NO:270), Figure 109 (SEQ ID NO:284), Figure 118 (SEQ ID NO:296), Figure 120 (SEQ ID NO:301), Figure 122 (SEQ ID NO:303), Figure 125 (SEQ ID NO:309), Figure 129 (SEQ ID NO:322), Figure 132 (SEQ ID NO:330), Figure 136 (SEQ ID NO:337), Figure 139 (SEQ ID NO:346), Figure 142 (SEQ ID NO:352), Figure 145 (SEQ ID NO:358), Figure 147 (SEQ ID NO:363), Figure 149 (SEQ ID NO:370), Figure 151 (SEQ ID NO:375), Figure 153 (SEQ ID NO:380), Figure 155 (SEQ ID NO:385), Figure 157 (SEQ ID NO:390), Figure 159 (SEQ ID NO:395), Figure 161 (SEQ ID NO:400), Figure 163 (SEQ ID NO:405), Figure 165 (SEQ ID NO:410), Figure 167 (SEQ ID NO:415), Figure 169 (SEQ ID NO:420), Figure 171 (SEQ ID NO:425), Figure 173 (SEQ ID NO:430), Figure 177 (SEQ ID NO:437), Figure 179 (SEQ ID NO:442), Figure 181 (SEQ ID NO:447), Figure 183 (SEQ ID NO:452), Figure 185 (SEQ ID NO:454), Figure 187 (SEQ ID NO:456), Figure 190 (SEQ ID NO:459), Figure 192 (SEQ ID NO:464), Figure 194 (SEQ ID NO:466), Figure 196 (SEQ ID NO:468), Figure 198 (SEQ ID NO:470), Figure 200 (SEQ ID NO:472), Figure 202 (SEQ ID NO:477), Figure 204 (SEQ ID NO:483), Figure 207 (SEQ ID NO:488), Figure 209 (SEQ ID NO:496), Figure 211 (SEQ ID NO:498), Figure 213 (SEQ ID NO:506), Figure 215 (SEQ ID NO:508), Figure 217 (SEQ ID NO:510), Figure 219 (SEQ ID NO:515), Figure 222 (SEQ ID NO:523) and Figure 225 (SEQ ID NO:526).

2. The nucleic acid sequence of Claim 1, wherein said nucleotide sequence comprises a nucleotide sequence selected from the group consisting of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:6), Figure 8 (SEQ ID NO:18), Figure 10 (SEQ ID NO:27), Figure 14 (SEQ ID NO:35), Figure 19 (SEQ ID NO:44), Figure 21 (SEQ ID NO:51), Figure 23 (SEQ ID NO:58), Figure 25 (SEQ ID NO:63), Figure 27 (SEQ ID NO:68), Figure 29 (SEQ ID NO:73), Figure 32 (SEQ ID NO:84), Figure 34 (SEQ ID NO:89), Figure 36 (SEQ ID NO:96), Figure 38 (SEQ ID NO:101), Figure 40 (SEQ ID NO:108), Figure 42 (SEQ ID NO:113), Figure 44 (SEQ ID NO:118), Figure 46 (SEQ ID NO:123), Figure 48 (SEQ ID NO:131), Figure 50 (SEQ ID NO:136), Figure 52 (SEQ ID NO:144), Figure 54 (SEQ ID NO:149), Figure 58 (SEQ ID NO:156), Figure 60 (SEQ ID NO:161), Figure 62 (SEQ ID NO:168), Figure 65 (SEQ ID NO:177), Figure 67 (SEQ ID NO:182), Figure 69 (SEQ ID NO:189), Figure 72 (SEQ ID NO:195), Figure 74 (SEQ ID NO:205), Figure 76 (SEQ ID NO:210), Figure 78 (SEQ ID NO:215), Figure 80 (SEQ ID NO:220), Figure 82 (SEQ ID NO:225), Figure 84 (SEQ ID NO:230), Figure 86 (SEQ ID NO:235), Figure 88 (SEQ ID NO:244), Figure 90 (SEQ ID NO:253), Figure 92 (SEQ ID NO:258), Figure 94

(SEQ ID NO:263), Figure 97 (SEQ ID NO:269), Figure 108 (SEQ ID NO:283), Figure 117 (SEQ ID NO:295), Figure 119 (SEQ ID NO:300), Figure 121 (SEQ ID NO:302), Figure 124 (SEQ ID NO:308), Figure 128 (SEQ ID NO:321), Figure 131 (SEQ ID NO:329), Figure 135 (SEQ ID NO:336), Figure 138 (SEQ ID NO:345), Figure 141 (SEQ ID NO:351), Figure 144 (SEQ ID NO:357), Figure 146 (SEQ ID NO:362), Figure 148 (SEQ ID NO:369), Figure 150 (SEQ ID NO:374), Figure 152 (SEQ ID NO:379), Figure 154 (SEQ ID NO:384), Figure 156 (SEQ ID NO:389), Figure 158 (SEQ ID NO:394), Figure 160 (SEQ ID NO:399), Figure 162 (SEQ ID NO:404), Figure 164 (SEQ ID NO:409), Figure 166 (SEQ ID NO:414), Figure 168 (SEQ ID NO:419), Figure 170 (SEQ ID NO:424), Figure 172 (SEQ ID NO:429), Figure 176 (SEQ ID NO:436), Figure 178 (SEQ ID NO:441), Figure 180 (SEQ ID NO:446), Figure 182 (SEQ ID NO:451), Figure 184 (SEQ ID NO:453), Figure 186 (SEQ ID NO:455), Figure 189 (SEQ ID NO:458), Figure 191 (SEQ ID NO:463), Figure 193 (SEQ ID NO:465), Figure 195 (SEQ ID NO:467), Figure 197 (SEQ ID NO:469), Figure 199 (SEQ ID NO:471), Figure 201 (SEQ ID NO:476), Figure 203 (SEQ ID NO:482), Figure 206 (SEQ ID NO:487), Figure 208 (SEQ ID NO:495), Figure 210 (SEQ ID NO:497), Figure 212 (SEQ ID NO:505), Figure 214 (SEQ ID NO:507), Figure 216 (SEQ ID NO:509), Figure 218 (SEQ ID NO:514), Figure 221 (SEQ ID NO:522) and Figure 224 (SEQ ID NO:525).

3. The nucleic acid of Claim 1, wherein said nucleotide sequence comprises a nucleotide sequence selected from the group consisting of the full-length coding sequence of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:6), Figure 8 (SEQ ID NO:18), Figure 10 (SEQ ID NO:27), Figure 14 (SEQ ID NO:35), Figure 19 (SEQ ID NO:44), Figure 21 (SEQ ID NO:51), Figure 23 (SEQ ID NO:58), Figure 25 (SEQ ID NO:63), Figure 27 (SEQ ID NO:68), Figure 29 (SEQ ID NO:73), Figure 32 (SEQ ID NO:84), Figure 34 (SEQ ID NO:89), Figure 36 (SEQ ID NO:96), Figure 38 (SEQ ID NO:101), Figure 40 (SEQ ID NO:108), Figure 42 (SEQ ID NO:113), Figure 44 (SEQ ID NO:118), Figure 46 (SEQ ID NO:123), Figure 48 (SEQ ID NO:131), Figure 50 (SEQ ID NO:136), Figure 52 (SEQ ID NO:144), Figure 54 (SEQ ID NO:149), Figure 58 (SEQ ID NO:156), Figure 60 (SEQ ID NO:161), Figure 62 (SEQ ID NO:168), Figure 65 (SEQ ID NO:177), Figure 67 (SEQ ID NO:182), Figure 69 (SEQ ID NO:189), Figure 72 (SEQ ID NO:195), Figure 74 (SEQ ID NO:205), Figure 76 (SEQ ID NO:210), Figure 78 (SEQ ID NO:215), Figure 80 (SEQ ID NO:220), Figure 82 (SEQ ID NO:225), Figure 84 (SEQ ID NO:230), Figure 86 (SEQ ID NO:235), Figure 88 (SEQ ID NO:244), Figure 90 (SEQ ID NO:253), Figure 92 (SEQ ID NO:258), Figure 94 (SEQ ID NO:263), Figure 97 (SEQ ID NO:269), Figure 108 (SEQ ID NO:283), Figure 117 (SEQ ID NO:295), Figure 119 (SEQ ID NO:300), Figure 121 (SEQ ID NO:302), Figure 124 (SEQ ID NO:308), Figure 128 (SEQ ID NO:321), Figure 131 (SEQ ID NO:329), Figure 135 (SEQ ID NO:336), Figure 138 (SEQ ID NO:345), Figure 141 (SEQ ID NO:351), Figure 144 (SEQ ID NO:357), Figure 146 (SEQ ID NO:362), Figure 148 (SEQ ID NO:369), Figure 150 (SEQ ID NO:374), Figure 152 (SEQ ID NO:379), Figure 154 (SEQ ID NO:384), Figure 156 (SEQ ID NO:389), Figure 158 (SEQ ID NO:394), Figure 160 (SEQ ID NO:399), Figure 162 (SEQ ID NO:404), Figure 164 (SEQ ID NO:409), Figure 166 (SEQ ID NO:414), Figure 168 (SEQ ID NO:419), Figure 170 (SEQ ID NO:424), Figure 172 (SEQ ID NO:429), Figure 176 (SEQ ID NO:436), Figure 178 (SEQ ID NO:441), Figure 180 (SEQ ID NO:446), Figure 182 (SEQ ID NO:451), Figure 184 (SEQ ID NO:453), Figure 186 (SEQ ID NO:455), Figure 189 (SEQ ID NO:458), Figure 191 (SEQ ID NO:463), Figure 193 (SEQ ID NO:465), Figure 195 (SEQ ID NO:467), Figure 197 (SEQ ID NO:469), Figure 199 (SEQ ID NO:471), Figure 201 (SEQ ID NO:476), Figure 203 (SEQ ID NO:482), Figure 206 (SEQ ID NO:487), Figure 208 (SEQ ID NO:495), Figure 210 (SEQ ID NO:497), Figure 212 (SEQ ID NO:505), Figure 214 (SEQ ID NO:507), Figure 216 (SEQ ID NO:509), Figure 218

(SEQ ID NO:514), Figure 221 (SEQ ID NO:522) or Figure 224 (SEQ ID NO:525).

4. Isolated nucleic acid which comprises the full-length coding sequence of the DNA deposited under accession number ATCC 209791, ATCC 209786, ATCC 209788, ATCC 209787, ATCC 209789, ATCC 209617, ATCC 209620, ATCC 209616, ATCC 209679, ATCC 209654, ATCC 209655, ATCC 209656, ATCC 209721, ATCC 209717, ATCC 209716, ATCC 209722, ATCC 209668, ATCC 209670, ATCC 209718, ATCC 209784, ATCC 209703, ATCC 209808, ATCC 209810, ATCC 209699, ATCC 209811, ATCC 209813, ATCC 209705, ATCC 209806, ATCC 209809, ATCC 209805, ATCC 209812, ATCC 209844, ATCC 209847, ATCC 209845, ATCC 209843, ATCC 209846, ATCC 209750, ATCC 209848, ATCC 209851, ATCC 209754, ATCC 209747, ATCC 209861, ATCC 209862, ATCC 209867, ATCC 209879, ATCC 209868, ATCC 209869, ATCC 209775, ATCC 209772, ATCC 209774, ATCC 209777, ATCC 209905, ATCC 209855, ATCC 209910, ATCC 209424, ATCC 209720, ATCC 209714, ATCC 209785, ATCC 209911, ATCC 209669, ATCC 209704, ATCC 209702, ATCC 209701, ATCC 209700, ATCC 209814, ATCC 209715, ATCC 209807, ATCC 209753, ATCC 209749, ATCC 209748, ATCC 209842, ATCC 209849, ATCC 209880, ATCC 209864, ATCC 209882, ATCC 209883, ATCC 209865, ATCC 209866, ATCC 209857, ATCC 209870, ATCC 209859, ATCC 209653, ATCC 209389, ATCC 209386, ATCC 203242, ATCC 203243, ATCC 209783, ATCC 209487 or ATCC 209680.

5. A vector comprising the nucleic acid of Claim 1.

6. The vector of Claim 5 operably linked to control sequences recognized by a host cell transformed with the vector.

7. A host cell comprising the vector of Claim 5.

8. The host cell of Claim 7 wherein said cell is a CHO cell.

9. The host cell of Claim 7 wherein said cell is an *E. coli*.

10. The host cell of Claim 7 wherein said cell is a yeast cell.

11. A process for producing a PRO polypeptides comprising culturing the host cell of Claim 7 under conditions suitable for expression of said PRO polypeptide and recovering said PRO polypeptide from the cell culture.

12. Isolated native sequence PRO polypeptide having at least 80% sequence identity to an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:7), Figure 9 (SEQ ID NO:19), Figure 11 (SEQ ID NO:28), Figure 15 (SEQ ID NO:36), Figure 20 (SEQ ID NO:45), Figure 22 (SEQ ID NO:52), Figure 24 (SEQ ID NO:59), Figure 26 (SEQ ID NO:64), Figure 28 (SEQ ID NO:69), Figure 30 (SEQ ID NO:74), Figure 33 (SEQ ID NO:85), Figure 35 (SEQ ID NO:90), Figure 37 (SEQ ID NO:97), Figure 39 (SEQ ID NO:102), Figure 41 (SEQ ID NO:109), Figure 43 (SEQ ID NO:114), Figure 45 (SEQ ID NO:119), Figure 47 (SEQ ID NO:124), Figure 49 (SEQ ID NO:132), Figure 51 (SEQ ID NO:137),

Figure 53 (SEQ ID NO:145), Figure 55 (SEQ ID NO:150), Figure 59 (SEQ ID NO:157), Figure 61 (SEQ ID NO:162), Figure 63 (SEQ ID NO:169), Figure 66 (SEQ ID NO:178), Figure 68 (SEQ ID NO:183), Figure 70 (SEQ ID NO:190), Figure 73 (SEQ ID NO:196), Figure 75 (SEQ ID NO:206), Figure 77 (SEQ ID NO:211), Figure 79 (SEQ ID NO:216), Figure 81 (SEQ ID NO:221), Figure 83 (SEQ ID NO:226), Figure 85 (SEQ ID NO:231), Figure 87 (SEQ ID NO:236), Figure 89 (SEQ ID NO:245), Figure 91 (SEQ ID NO:254), Figure 93 (SEQ ID NO:259), Figure 95 (SEQ ID NO:264), Figure 98 (SEQ ID NO:270), Figure 109 (SEQ ID NO:284), Figure 118 (SEQ ID NO:296), Figure 120 (SEQ ID NO:301), Figure 122 (SEQ ID NO:303), Figure 125 (SEQ ID NO:309), Figure 129 (SEQ ID NO:322), Figure 132 (SEQ ID NO:330), Figure 136 (SEQ ID NO:337), Figure 139 (SEQ ID NO:346), Figure 142 (SEQ ID NO:352), Figure 145 (SEQ ID NO:358), Figure 147 (SEQ ID NO:363), Figure 149 (SEQ ID NO:370), Figure 151 (SEQ ID NO:375), Figure 153 (SEQ ID NO:380), Figure 155 (SEQ ID NO:385), Figure 157 (SEQ ID NO:390), Figure 159 (SEQ ID NO:395), Figure 161 (SEQ ID NO:400), Figure 163 (SEQ ID NO:405), Figure 165 (SEQ ID NO:410), Figure 167 (SEQ ID NO:415), Figure 169 (SEQ ID NO:420), Figure 171 (SEQ ID NO:425), Figure 173 (SEQ ID NO:430), Figure 177 (SEQ ID NO:437), Figure 179 (SEQ ID NO:442), Figure 181 (SEQ ID NO:447), Figure 183 (SEQ ID NO:452), Figure 185 (SEQ ID NO:454), Figure 187 (SEQ ID NO:456), Figure 190 (SEQ ID NO:459), Figure 192 (SEQ ID NO:464), Figure 194 (SEQ ID NO:466), Figure 196 (SEQ ID NO:468), Figure 198 (SEQ ID NO:470), Figure 200 (SEQ ID NO:472), Figure 202 (SEQ ID NO:477), Figure 204 (SEQ ID NO:483), Figure 207 (SEQ ID NO:488), Figure 209 (SEQ ID NO:496), Figure 211 (SEQ ID NO:498), Figure 213 (SEQ ID NO:506), Figure 215 (SEQ ID NO:508), Figure 217 (SEQ ID NO:510), Figure 219 (SEQ ID NO:515), Figure 222 (SEQ ID NO:523) and Figure 225 (SEQ ID NO:526).

13. Isolated PRO polypeptide having at least 80% sequence identity to the amino acid sequence encoded by the nucleotide deposited under accession number ATCC 209791, ATCC 209786, ATCC 209788, ATCC 209787, ATCC 209789, ATCC 209617, ATCC 209620, ATCC 209616, ATCC 209679, ATCC 209654, ATCC 209655, ATCC 209656, ATCC 209721, ATCC 209717, ATCC 209716, ATCC 209722, ATCC 209668, ATCC 209670, ATCC 209718, ATCC 209784, ATCC 209703, ATCC 209808, ATCC 209810, ATCC 209699, ATCC 209811, ATCC 209813, ATCC 209705, ATCC 209806, ATCC 209809, ATCC 209805, ATCC 209812, ATCC 209844, ATCC 209847, ATCC 209845, ATCC 209843, ATCC 209846, ATCC 209750, ATCC 209848, ATCC 209851, ATCC 209754, ATCC 209747, ATCC 209861, ATCC 209862, ATCC 209867, ATCC 209879, ATCC 209868, ATCC 209869, ATCC 209775, ATCC 209772, ATCC 209774, ATCC 209777, ATCC 209905, ATCC 209855, ATCC 209910, ATCC 209424, ATCC 209720, ATCC 209714, ATCC 209785, ATCC 209911, ATCC 209669, ATCC 209704, ATCC 209702, ATCC 209701, ATCC 209700, ATCC 209814, ATCC 209715, ATCC 209807, ATCC 209753, ATCC 209749, ATCC 209748, ATCC 209842, ATCC 209849, ATCC 209880, ATCC 209864, ATCC 209882, ATCC 209883, ATCC 209865, ATCC 209866, ATCC 209857, ATCC 209870, ATCC 209859, ATCC 209653, ATCC 209389, ATCC 209386, ATCC 203242, ATCC 203243, ATCC 209783, ATCC 209487 or ATCC 209680.

14. A chimeric molecule comprising a polypeptide according to Claim 12 fused to a heterologous amino acid sequence.

15. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is an epitope

tag sequence.

16. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is a Fc region of an immunoglobulin.

17. An antibody which specifically binds to a PRO polypeptide according to Claim 12.

18. The antibody of Claim 17 wherein said antibody is a monoclonal antibody.

19. An isolated nucleic acid molecule which has at least 80% sequence identity to a nucleic acid which comprises a nucleotide sequence selected from the group consisting of that shown in Figure 5 (SEQ ID NO:8), Figure 6 (SEQ ID NO:9), Figure 7 (SEQ ID NO:10), Figure 12 (SEQ ID NO:29), Figure 13 (SEQ ID NO:30), Figure 16 (SEQ ID NO:37), Figure 17 (SEQ ID NO:38), Figure 18 (SEQ ID NO:39), Figure 31 (SEQ ID NO:75), Figure 64 (SEQ ID NO:170), Figure 71 (SEQ ID NO:191), Figure 96 (SEQ ID NO:265), Figure 99 (SEQ ID NO:271), Figure 100 (SEQ ID NO:272), Figure 101 (SEQ ID NO:273), Figure 102 (SEQ ID NO:274), Figure 103 (SEQ ID NO:275), Figure 104 (SEQ ID NO:276), Figure 105 (SEQ ID NO:277), Figure 106 (SEQ ID NO:278), Figure 107 (SEQ ID NO:279), Figure 110 (SEQ ID NO:285), Figure 111 (SEQ ID NO:286), Figure 112 (SEQ ID NO:287), Figure 113 (SEQ ID NO:288), Figure 114 (SEQ ID NO:289), Figure 115 (SEQ ID NO:290), Figure 116 (SEQ ID NO:291), Figure 123 (SEQ ID NO:304), Figure 126 (SEQ ID NO:310), Figure 127 (SEQ ID NO:311), Figure 130 (SEQ ID NO:323), Figure 133 (SEQ ID NO:331), Figure 134 (SEQ ID NO:332), Figure 137 (SEQ ID NO:338), Figure 140 (SEQ ID NO:347), Figure 143 (SEQ ID NO:353), Figure 174 (SEQ ID NO:431), Figure 175 (SEQ ID NO:432), Figure 188 (SEQ ID NO:457), Figure 205 (SEQ ID NO:484), Figure 220 (SEQ ID NO:516), Figure 223 (SEQ ID NO:524), Figure 226 (SEQ ID NO:527), Figure 227 (SEQ ID NO:528) and Figure 228 (SEQ ID NO:529).